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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,951	02/05/2006	Maisam Mitalipova	18377-0061	8860

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EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1649	

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11/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/539,951	MITALIPOVA ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-51 and 53-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-51 and 53-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed on 7/31/08 has been entered.

2. The rejection of claims 46-53 & 55 under 35 U.S.C. 112, second paragraph, as being indefinite or incomplete is withdrawn due to the amendment or cancellation of the claims.

3. Applicant's arguments filed 7/31/08 have been fully considered but they are not deemed to be persuasive.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claim 54 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite or incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper No: 20080710, and as follows.

The term "essentially" in claim 54 is still a relative term which renders the claim indefinite. The term "essentially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be

reasonably apprised of the scope of the invention. In other words, it is unclear when medium is "essentially" serum-free, versus at what point medium is no longer "essentially" serum-free.

In contrast to Applicants' arguments, claim 56 is not reasonably limited to medium where only LIF is at a *de minimus* concentration. Nor does the specification clearly provide a closed ended definition for this "relative" term. In contrast, the specification includes "or a reduced amount" in the definition for "essentially", in which it therefore remains unclear under what conditions "serum" is absent versus only being "reduced". Thus, Applicants' arguments are not persuasive.

6. Claims 46-51 & 53-55 stand rejected under 35 U.S.C. 102(e) as being anticipated by Carpenter (1999, US Patent 5,968,829; IDS Ref #8), for the reasons made of record in Paper No: 20080710, and as follows.

Applicants argue on pages 5-6 of the response that "the Carpenter '829 patent describes 'neural cells' derived from human fetal forbrain (hFBr), and not derived *in vitro* from human embryonic stem cells, as in amended claim 46", and that "it is the human fetal forebrain cells which were passaged every 6-21 days depending upon the mitogens used and the seeding density…". Applicants then state "[t]hat is, the 9FBr human neural cells were not passaged". The issue is simple. The claims are directed to a product, isolated neural progenitor cells, not a method of making such cells, in which product-by-process limitations that do not change the product hold no patentable weight. Second, Carpenter's method of culturing neural stem/ progenitor cells does not mean no neural stem/progenitor cells are present in their initial cultures, which were then "passaged every 6-21 days depending upon the mitogens used and the seeding

density", as Applicants acknowledge, because human fetal tissue inherently contain these cells, by definition, and because this is from where these "nestin-positive" cells were "derived", and then propagated. Therefore, in contrast to Applicants' conclusion, Carpenter does teach each and every relevant limitation claimed. Thus, Applicants' arguments are not persuasive.

In summary, Carpenter teach "nestin"-positive neural stem/progenitor cells in serum-free DMEM/F-12 medium comprising the low molecular weight component, insulin (which comprises proline), and the neural inducing factors, EGF, bFGF, PDGF, NGF & LIF, which were also proliferated up to 130 cell divisions and 90 days in culture (e.g., cols. 2-4 & 8-9, Figs. 2B & 3; as it relates to claims 46, 47-50 & 54). In that the MEDII medium is defined in claim 55 to only consist of at least one of the components (a)-(f), the limitations for being stabilized by MEDII medium (i.e., a process) throughout the claims is also met.

Again, the issue remains that if the product in a product-by-process claim (i.e., "an isolated neural progenitor cell"), which is then stabilized or made by any process that results in a product that is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe.,* 227 USPQ 964, 966 (Fed. Cir. 1985): *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983).

It has further been established by the courts that a product (i.e., the neural precursor cell product) inherently possesses characteristics of that product (i.e., ability to differentiate into more than one type of further differentiated neural cell), and that:

"the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Accordingly, since the issue in the present appeal is whether the prior art factor is identified or patently indistinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved". *Ex parte Gray,* 10 USPQ 2d 1922 (1989); *In re Best,* 195 USPQ 430 (CCPA 1976).

The court in *In re Crish*, 73 USPQ2d 1364 (Fed. Cir. 2004), also held that "... the [further] identification and characterization of a [previously known] prior art material... does not make it novel".

Lastly, it is noted that the courts have held that when the prior art product reasonably appears to be the same as that claimed, but differs by process in which it is produced, a rejection of this nature is eminently fair and the burden is upon the appellants to prove, by comparative evidence, a patentable difference (*In re Brown*, 173 USPQ 685 (1972)).

7. Claims 46-51 & 53-55 stand rejected under 35 U.S.C. 102(e) as being anticipated by Bresagen Limited/ Rathjen et al (WO 01/51611; IDS Ref #14), for the reasons made of record in Paper No: 20080710, and as follows.

Applicants argue on page 7 of the response that "the claim 46 has been amended to further clarify the invention by explicitly reciting the claimed composition comprises an isolated nestin-positive neural progenotr cell...", and that "the Rathjen publication describes nestin-positive neural ectoderm/EPL embryoid (EBs) in serum-free HepG2 conditioned MEDII that are derived from mouse embryonic stem cells". In contrast to Applicants' assertions, no where in Rathjen et al is it stated that their neural progenitor cells are limited to mouse derived cells. In contrast, page 2 of WO 01/51611, for example, states:

> In the human and in other mammals, formation of the blastocyst, including development of ICM cells and their progression to pluripotent cells of the primitive ectoderm, and subsequent differentiation to form the embryonic germ layers and differentiated cells; follow a similar developmental process.

Therefore, one reasonably would interpret the teachings of Rathjen as a teaching for making mammalian neural stem/progenitor cells *in vitro* from any mammalian embryonic tissue, including human embryos; especially when page 5 of '611 further states that "[i]t is an object of the present invention to overcome, or at least alleviate, one or more of the difficulties or deficiencies associated with the prior art", in which both rodent and human neural stem cells are previously discussed. Thus, Applicants' arguments are not persuasive.

In summary, Rathjen et al teach compositions comprising mammalian, rodent and human "nestin"-positive neuroectoderm / EPL embryoid bodies/ neural stem/progenitor cells in serum-free HepG2- conditioned MEDII medium (e.g., pgs. 7, 9, 11, 14, 28, 33, 37 & 47; as it relates to claims 46 & 52-55), in which WO99/53021 (IDS Ref #18) is incorporated by reference in '611 and states that "EPL cell morphology could be maintained with extended culture of greater than 40 passages, or 100 days (data not shown)" (pg. 46 of '021). Thus, the process limitations of claims 47-50 are also anticipated. In that contact with MEDII does not reasonably change the nestin positive neural cells of Rathjen even after "one year", the limitations of claim 51 are further anticipated, because if the product in a product-by-process claim (i.e., a "an isolated neural progenitor cell"), which is then stabilized or made by any process that results in a product that is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process (i.e., as it relates to claim 51). *In re Thorpe.,* 227 USPQ 964, 966 (Fed. Cir. 1985): *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983).

Lastly, it is noted that the courts have held that when the prior art product reasonably appears to be the same as that claimed, but differs by process in which it is produced, a rejection

of this nature is eminently fair and the burden is upon the appellants to prove, by comparative evidence, a patentable difference (*In re Brown*, 173 USPQ 685 (1972)).

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Stucker, can be reached on (571) 272-0911. The fax phone number for this Group is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Robert C. Hayes/
Primary Examiner, Art Unit 1649
November 12, 2008